POLICY AND PROCEDURES

OFFICE OF NEW DRUGS

Procedures for Completing and Processing the Form "Annual Status Report Review Form: PMR and PMC Summary"

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PURPOSE

This MAPP describes procedures to be used by Office of New Drugs (OND), Office of New Drug Quality Assurance (ONDQA), and Office of Biological Products (OBP) staff to:

- Verify an applicant's reported status and explanation of status of postmarketing requirements (PMRs) and postmarketing commitments (PMCs) by completing the form "Annual Status Report Review Form: PMR and PMC Summary" (ASR Review Form)

- Process the form in the document management system

BACKGROUND

- PMRs/PMCs are studies or clinical trials that are conducted by the applicant after the Food and Drug Administration (FDA) has approved a drug for marketing or licensing.[1] These studies or trials can be either required by regulation or statute (PMRs) or agreed upon by the FDA and the applicant (PMCs). (See the Definitions section.)

- Section 130(a) of the Food and Drug Administration Modernization Act of 1997 (FDAMA) amended the Federal Food, Drug, and Cosmetic Act (the FD&C Act) by adding a new provision requiring reports of certain postmarketing studies for human drug and biological products (section 506B of the FD&C Act (21 U.S.C. 356b)).[2] Section 506B of the FD&C Act provides the FDA with additional authority to monitor the progress of a PMR/PMC[3] that an applicant has been required or has agreed to conduct by requiring the applicant to submit an annual report that provides information on the status of the PMR/PMC. This report must also include the reasons, if any, for failure to complete the requirement/commitment. This provision is implemented at 21 CFR 314.81(b)(2)(vii) and 601.70. The regulations went into effect on April 30, 2001 (66 FR 10815).

- The status of PMCs not subject to the reporting requirements of section 506B of the FD&C Act, primarily PMCs related to chemistry, manufacturing, and controls (CMC) changes, are not required to be included in annual status reports (ASRs) required under section 130(a) of FDAMA. The status of CMC PMCs must be included in a separate section of the new drug application (NDA) annual report as required under 21 CFR 314.81(b)(2)(viii), or for biologic products in the annual report of changes to a biologics license application (BLA) required under 21 CFR 601.12. These reports should be reviewed by the appropriate ONDQA or OBP reviewer.[4]

[1] For the purposes of this MAPP, all references to *drugs* include both human drugs and therapeutic biological products unless otherwise specified.

[2] 21 CFR 314.81(b)(2)(vii) and 601.70 refer to studies/trials concerning clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology.

[3] Although reporting under section 506B of the FD&C Act, as required under 21 CFR 314.81(b)(2)(vii), refers only to postmarketing commitments, some of these commitments are required under the Pediatric Research Equity Act (PREA) (21 CFR 314.55(b) and 601.27(b)), the animal efficacy rule (21 CFR 314.610(b)(1) and 601.91(b)(1)), accelerated approval (21 CFR 314.510 and 601.41), and the Food and Drug Administration Amendments Act of 2007 (FDAAA) (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)) and are now referred to as PMRs.

[4] See MAPP 5310.6 *Procedures for Assessing Chemistry, Manufacturing, and Controls Data in NDA Annual Reports*.

- Effective March 25, 2008, section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) created section 505(o) of the FD&C Act, which authorizes the FDA to require certain postmarketing safety studies/clinical trials and requires applicants to submit a timetable for completion of each study/clinical trial. Applicants are also required to periodically report on each safety study/clinical trial required or otherwise undertaken to investigate a safety issue. Submission of the annual report on the status of PMRs/PMCs required under section 506B may also satisfy the periodic reporting requirements for PMRs under FDAAA.

- Effective March 25, 2008, section 901 of FDAAA created section 505-1 of the FD&C Act, which authorizes the FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if such a strategy is necessary to ensure that the benefits of the drug outweigh the risks, and to require assessments of an approved REMS. According to 505-1(g)(3)(B) and (C), assessments must include information on the status of any postapproval study or clinical trial required under section 505(o) (FDAAA PMR) or otherwise undertaken to investigate a safety issue. Applicants may refer to the most recent annual report information on the status of PMRs/PMCs required under section 506B (with any material or significant updates to the status information since the annual report was prepared) to satisfy this requirement.

- The ASRs required under section 130(a) of FDAMA are due each year within 60 days of the anniversary of U.S. drug approvals. The applicant must continue to report on the status of the PMR/PMC until it is notified in writing that the PMR/PMC has been fulfilled or released. This provision applies to requirements and commitments made before or after enactment of FDAMA.

- The FDA reviews the ASRs and then updates the status and other information in the PMR/PMC database.[5] The FDA uses the database to track PMR/PMC status and as a data source for certain information that is displayed on an FDA public Web site.[6] The FDA also publishes PMR/PMC data annually in the *Federal Register* to meet its obligations for public disclosure of information required under section 506B(b) and (c) of the FD&C Act.

[5] The PMR/PMC database refers to the data management system used in the Center for Drug Evaluation and Research (CDER) to capture and track all PMRs/PMCs.

[6] See http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Post-marketingPhaseIVCommitments/default.htm.

- The FDA has proposed in guidance that we will review an applicant's annual postmarketing requirement and commitment status report within 3 months of receipt to determine whether we agree with the applicant's reported status and explanation of status for each open PMR/PMC. The information needed to verify the accuracy of the applicant's reported status and explanation of status for open PMRs/PMCs is captured on the ASR Review Form, which may be found in the Center for Drug Evaluation and Research (CDER) Standard Templates repository.

POLICY

- OND staff, in consultation with other review staff (e.g., Office of Clinical Pharmacology (OCP), Office of Surveillance and Epidemiology (OSE)) as needed, will review ASRs (when submitted for applications with open PMRs/PMCs) and complete the ASR Review Form to verify the reported status and explanation of status of PMRs and PMCs (see Attachments 1 and 2).

- ONDQA and OBP staff will review ASRs with open CMC PMRs/PMCs and complete the ASR Review Form to verify the reported status and explanation of the status of CMC PMCs (see Attachments 1 and 2).

- If multiple reviews of the ASR are conducted by individual discipline-specific reviewers (e.g., OND, OCP, OSE, ONDQA, and OBP), the collated assessments may be combined into a single ASR Review Form and archived in the document management system. If not combined, each individual reviewer may process his or her own ASR Review Form in the document management system.

- Review staff will process the ASR Review Form (whether combined or separate forms) in the document management system within 3 months of FDA receipt of the ASR (see Attachment 2).

- For applications with PMRs required under FDAAA, including CMC PMRs, all communications to the applicant will be coordinated with the OND division safety regulatory project manager (SRPM), OND division deputy director for safety (DDS), and, if appropriate, the Office of Compliance.

- The ASR Review Form will be completed and processed at the discretion (i.e., responsibilities and roles) of the review division.

RESPONSIBILITIES AND PROCEDURES

The OND Regulatory Project Manager will:

- Confirm, for applications with open PMRs/PMCs, that the ASR was submitted

- Notify the PMR/PMC tracking coordinator that the ASR was received

- Assign the ASR, based on the current reviewer assignments for the application, to the appropriate reviewer or reviewers to include a discipline-specific review of the ASR (e.g., CMC PMRs/PMCs should be assigned to the appropriate ONDQA or OBP reviewer)

- Ensure that each assigned reviewer(s) and the PMR/PMC tracking coordinator promptly receives a copy of the ASR

The PMR/PMC Tracking Coordinator will:

- Confirm that the ASR addresses all the open PMRs/PMCs established under the application, including supplements (e.g., by comparing the ASR to a list of open PMRs/PMCs for the referenced application obtained from the PMR/PMC database). (Note: For NDAs, the status of open CMC PMCs may be reported by the applicant in a separate section of the annual report. Therefore, if the open CMC PMCs are not listed with the other PMRs/PMCs, the PMR/PMC tracking coordinator should look elsewhere in the annual report before assuming that the ASR is incomplete.)

- Communicate deficiencies (e.g., missing or incomplete ASRs) to the applicant via PMR/PMC Dunner letters or other correspondence, as appropriate.

- Notify the assigned reviewer(s) that the ASR is complete and ready for review.

- Review and verify the information provided by the applicant in the ASR regarding the PMRs/PMCs if the PMR/PMC tracking coordinator also assumes the reviewer role. (Note: The PMR/PMC tracking coordinator may also assume the reviewer role in this process depending on the discretionary designation of responsibilities and roles at the division level.)

- Monitor that verification of the ASR and completion of the ASR Review Form are accomplished within the 3-month time frame.

- Collate, as appropriate, the individual reviewer assessments of the reported status and explanation of status for open PMRs/PMCs. Separate ASR Review Forms may be completed by other discipline-specific reviewers.

- After completion of the ASR Review Form(s), communicate with the applicant if the PMR/PMC statuses and/or explanations of status reported in its ASR are incorrect or are not supported by adequate information. Communicate the correction(s) as well as the rationale behind the correction(s). (See Attachments 1 and 2.)

  Note: For applications with PMRs required under FDAAA, including CMC PMRs, the PMR/PMC tracking coordinator will coordinate all communications with the SRPM, DDS, and, if appropriate, the Office of Compliance.

- Generate and complete the ASR Review Form. Enter the applicant-reported status, actual status, and explanation of actual status for each open PMR/PMC in Section B of the form. If the annual status report is incomplete, Section B of the form may be used to provide this information for any open PMRs/PMCs that are not, but should be, listed in the annual status report (see Attachments 1 and 2).

- Process the ASR Review Form in the document management system with the appropriate sign-off (see the Policy section). Before checking the document into the document management system or filing it in the BLA archival files, attach a copy of the applicant's PMR/PMC ASR (not the entire annual report) and form FDA 2252 ("Transmittal of Annual Report for Drugs and Biologics for Human Use") to the ASR Review Form. For paper submissions, this process will require scanning the original document.

- Ensure the appropriate FDA staff receives the completed form(s) and FDA communications to update the PMR/PMC database in a timely manner.

The Reviewers will:

- Review and verify the information provided by the applicant in the ASR regarding the PMRs/PMCs that are specific to the reviewer's discipline. (Note: The PMR/PMC tracking coordinator may also assume the reviewer role in this process depending on the discretionary designation of responsibilities and roles at the division level.)

- Notify the PMR/PMC tracking coordinator if any reported status categories are not supported by adequate information.

- Do one of the following depending on the discretionary designation of responsibilities and roles at the division level:

  – Provide completed comments to the PMR/PMC tracking coordinator who will complete and process the form (a formal written review of the ASR is not required)

  OR

  – Generate and complete the ASR Review Form. Enter the applicant-reported status, actual status, and explanation of actual status for each open PMR/PMC in Section B of the form. If the annual status report is incomplete, Section B of the form may be used to provide this information for any open PMRs/PMCs that are not, but should be, listed in the annual status report (see Attachments 1 and 2)

  AND

  - Process the ASR Review Form in the document management system with the appropriate sign-off (see the Policy section). Before checking the document into the document management system or filing it in the BLA archival files, attach a copy of the applicant's PMR/PMC ASR (not the entire annual report) and form FDA 2252 ("Transmittal of Annual Report for Drugs and Biologics for Human Use") to the ASR Review Form. For paper submissions, this process will require scanning the original document.

- Complete and process the ASR Review Form in the document management system or file the form in the BLA archival files within 3 months of FDA receipt of the ASR. The time it takes to review the ASR, collate comments, and generate and process the form should be considered in the overall time frame for completion.

REFERENCES

- Federal Food, Drug, and Cosmetic Act, section 506B (http://www.fda.gov/opacom/laws/fdcact/fdcact5a.htm), and section 505(o)(3), created by section 901 of the Food and Drug Administration Amendments Act of 2007 (http://www.fda.gov/oc/initiatives/advance/fdaaa.html)

- 21 CFR 314.81(b)(2), Other postmarketing reports

- 21 CFR 601.70, Annual progress reports of postmarketing studies

- 21 CFR 601.12, Changes to an approved application

- Guidance for industry *Postmarketing Studies and Clinical Trials — Implementation of Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act* (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm)

- Guidance for industry *Reports on the Status of Postmarketing Study Commitments — Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997* (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm)

- MAPP 5310.6 *Procedures for Assessing Chemistry, Manufacturing, and Controls Data in NDA Annual Reports* (http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm)

- MAPP 6010.2R *Responsibilities for Tracking and Communicating the Status of Postmarketing Requirements and Commitments* (http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm)

- MAPP 6010.9 *Procedures and Responsibilities for Developing Postmarketing Requirements and Commitments* (http://www.fda.gov/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/default.htm)

DEFINITIONS

- **506B-Reportable Postmarketing Requirements and Commitments** — Postmarketing studies or clinical trials concerning clinical safety, clinical efficacy, clinical pharmacology, or nonclinical toxicology that applicants have agreed upon in writing or are required to conduct.[7] The FDA is required to make certain information publicly available about these studies/clinical trials.

- **Annual Status Reports (ASRs) of Postmarketing Requirements and Commitments** — A progress report submitted annually for applications with certain open postmarketing requirements and commitments (e.g., clinical safety, clinical efficacy, clinical pharmacology, and nonclinical toxicology studies/trials). For NDAs, the ASR is submitted as a section within the annual report; for BLAs, the ASR is submitted as a separate report. The report must include all the information required under 21 CFR 314.81(b)(2) and 601.70.

- **CDER Standard Templates (CST)** — A collection of internally developed templates used by staff in CDER new drug review divisions to generate standardized letters and forms.

- **Postmarketing Commitment (PMC) —** Any study or clinical trial that an applicant has *agreed*, in writing, to conduct after approval of a marketing or licensing application or supplement that is *not* a PMR (see below).

- **Postmarketing Requirement (PMR)** — Any study or clinical trial that an applicant is required to conduct after approval of a marketing or licensing application or a supplement. Studies or clinical trials may be required under the Pediatric Research Equity Act (21 CFR 314.55(b) and 601.27(b)), the animal efficacy rule (21 CFR 314.610(b)(1) and 601.91(b)(1)), accelerated approval (21 CFR 314.510 and 601.41), or FDAAA (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)).

[7] 506B reporting, as required under 21 CFR 314.81(b)(2)(vii), refers to *postmarketing study commitments*, even though it includes studies and trials required under PREA (21 CFR 314.55(b) and 601.27(b)), the animal efficacy rule (21 CFR 314.610(b)(1) and 601.91(b)(1)), accelerated approval (21 CFR 314.510 and 601.41), and FDAAA (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)) that are now referred to as *postmarketing requirements*. Similarly, this reporting often refers to *study*; FDAAA distinguishes between study and *clinical trial*. Finally, 506B reporting includes *clinical safety* PMCs; studies or clinical trials that concern serious safety risks will now be required under FDAAA. Section 130 of FDAMA amended the FD&C Act to add section 506B and predates FDAAA. The definition of postmarketing commitments has been revised in accordance with FDAAA.

- **PMR/PMC Schedule Milestones** — The specific milestone dates set forth as part of a PMR/PMC for conducting and completing a PMR/PMC that must be reported annually. The following milestone dates should be included in the schedule:

  – Final protocol submission date
  – Study/clinical trial completion date
  – Final report submission date

- **PMR/PMC Tracking Coordinator —** One or more OND review division staff members, generally an OND review division SRPM, with the role of ensuring that the review team is kept informed of PMR/PMC schedule milestones, verifying PMR/PMC information for accuracy, and monitoring whether expected activities are conducted according to the timelines specified in the letter and in CDER policy documents (e.g., applicant submissions and FDA review). The PMR/PMC tracking coordinator assumes primary responsibility for corresponding with the applicant regarding PMR/PMC *process* issues. The tracking coordinator's responsibilities generally occur after approval.

- **Regulatory Project Manager (RPM) —** The OND division review team regulatory project manager (RPM) assigned to an application. The OND RPM has the primary responsibility for coordinating with the review team and corresponding with the applicant regarding PMR/PMC *content* issues.

- **Reviewer —** Discipline reviewer assigned to a drug (e.g., clinical, clinical pharmacology, nonclinical toxicology, safety-related disciplines, quality, biostatistics).

SUMMARY OF CHANGES

- This MAPP was revised to remove references to outdated data management and letter template systems; to include additional background information describing the FDA's new authority to require postmarketing safety studies and clinical trials under section 505(o) of the FD&C Act; to reflect the new PMR terminology; to add new references relevant to PMR/PMC tracking; and to update the ASR Review Form and instructions to more clearly capture PMR/PMC information.

EFFECTIVE DATE

This MAPP is effective upon date of publication.

CHANGE CONTROL TABLE

Effective Date	Revision Number	Revisions
3/16/05	Initial	n/a
10/26/11	Rev. 1	Removes references to outdated data management and letter template systems; includes additional background information describing the FDA's new authority to require postmarketing safety studies and clinical trials under section 505(o) of the FD&C Act; reflects the new PMR terminology; adds new references relevant to PMR/PMC tracking; updates the ASR Review Form and instructions to more clearly capture PMR/PMC information

ATTACHMENT 1
Annual Status Report Review Form: PMR and PMC Summary

This form is solely intended to verify the information provided by applicants in annual status reports (ASR) for postmarketing requirements/commitments. The form should address all open postmarketing requirements/commitments established under the application(s) whether or not they are subject to posting publicly on the Web site. For instructions for completing this form, please reference the corresponding instructional document or MAPP 6004.2 Rev. 1 *Procedures for Completing and Processing the Form "Annual Status Report Review Form: PMR and PMC Summary."*

ASR submitted electronically? ☐Y / ☐N
ASR/Form 2252 attached? ☐Y / ☐N

Status Report Reviewer/Division	REVIEWER NAME DIVISION NAME
Regulatory Project Manager	NAME
Safety RPM	NAME
Clinical Reviewer	NAME
Nonclinical Reviewer	NAME
Summary Sheet Completed	DATE

SECTION A: Application Information

NDA/BLA	######
Drug	NAME
Applicant	NAME
Supporting Document Number/ Submission Tracking Number	####
Status Report Received	DATE

SECTION B: Verification of the Reported Status [*Complete for each <u>open</u> requirement/commitment.*][8]

NDA, BLA, or Supplement #, or Postapproval Letter Date	PMR/PMC Set Number	PMR/PMC Number	Applicant-Reported Status	Actual Status per FDA Review	Revised Schedule Milestones	Explanation of Actual Status[1]
NDA ######, S-### **<u>or</u>** BLA ######\####**<u>or</u>** LETTER DATE	####	##	STATUS	STATUS	Y/N	EXPLANATION OF STATUS AND REASON FOR DISAGREEMENT, IF ANY

[1] See ASR Review Form: Instructions for Use. The explanation of actual status should not include proprietary information (e.g., IND numbers, personal privacy information, or references to unapproved formulations of the same drug or other unapproved drug products).

Disagreements in reported status communicated to Applicant? ☐Y/ ☐N

[8] For the column, Explanation of Actual Status, see Attachment 2, ASR Review Form: Instructions for Use. The explanation of actual status should not include proprietary information (e.g., IND numbers, personal privacy information, or references to unapproved formulations of the same drug or other unapproved drug products).

ATTACHMENT 2
Annual Status Report Review Form: PMR and PMC Summary (ASR Review Form) Instructions for Use

This form must be completed for all applications with open postmarketing requirements (PMRs) and postmarketing commitments (PMCs), including chemistry, manufacturing, and controls (CMCs), reported in the annual report (for new drug applications (NDAs)) or in a stand-alone "Status report of postmarketing requirements and commitments" (for biologics license applications (BLAs)). You do not need to complete this form for an application's annual report when there are no open PMRs or PMCs for the application. Note that the CMC PMCs are reported in another section of the NDA annual report or in the annual report of changes to a BLA rather than in the annual status report (ASR).

The appropriate ONDQA or OBP review division is responsible for completing an ASR Review Form for CMC PMCs. The appropriate OND review division is responsible for completing an ASR Review Form for non-CMC PMCs and for all PMRs.

Electronic submission: Indicate whether or not the annual report was submitted electronically.

Status report attached to form: Indicate whether or not the ASR (and form FDA 2252 for paper submissions) is attached electronically to this form.

Reviewer/division: Enter the name and division of the person who is completing this form. Names/divisions of individual reviewers who contributed comments to complete the form may also be captured here.

SECTION A: Application Information: Provide identifying information including the application number, drug name, applicant name, supporting document or submission tracking number, and receipt date (i.e., document room stamp date) in the appropriate fields.

SECTION B: Verification of the Reported Status: Provide the applicant-reported status, actual status, and explanation of actual status for each open PMR/PMC in the ASR.

Applicants should include all open PMRs and 506B PMCs in the ASR. Applicants are not required to report on non-506B (CMC) PMCs or closed (fulfilled or released) PMRs and PMCs in ASRs. However, you may use this section of the form to also list any open PMRs/PMCs (including CMC PMCs) that were not reported in the ASR but may have been reported in other sections of the annual report. Add rows as needed by pressing the Tab key from the last field (bottom-right) of the table.

NDA, BLA, or Supplement Number, or Postapproval Letter Date: Identify the application approval date or postapproval letter date in which the requirement or commitment was established. For example, if the PMR/PMC was included in the original NDA's approval letter, enter *N-000*. If the PMR/PMC was included in an approval letter for supplemental application number xxx, enter *S-xxx*. If the PMR/PMC originated in a separate postapproval letter, enter the date of that letter, and for BLAs also include the submission tracking number.

PMR/PMC Set Number: Enter the requirement/commitment set number as it appears in the PMR/PMC database. Note that BLAs do not currently include a PMR/PMC set number.

PMR/PMC Number: Enter the requirement/commitment number as it appears in the PMR/PMC database. An entry for each open PMR/PMC reported on in the ASR should be listed here. Note that updates to the database rely on identifying PMRs/PMCs by specific PMR/PMC set numbers and PMR/PMC numbers. Therefore, please provide the specific PMR/PMC numbers in this column even if the applicant did not provide them in the ASR.

PMR/PMC Status

One *and only one* status should be assigned to each PMR/PMC. The status categories are defined as follows:

Open Status Categories*:*

- *Pending* — The study or clinical trial has not been initiated (i.e., no subjects have been enrolled or animals dosed), but does not meet the criterion for *delayed* (i.e., the *original* projected date for initiation of subject accrual or initiation of animal dosing has not passed).

- *Ongoing* — The study or clinical trial is proceeding according to, or is ahead of, the *original* schedule. The FDA considers a study/clinical trial to be *ongoing* until a final report is submitted to the FDA, as long as the activities are proceeding according to the *original* schedule. If subject accrual or animal dosing has started but is not complete, and the projected date for completion of that milestone has passed, the study/clinical trial should be categorized as *delayed*.

- *Delayed* — The progression of the study/clinical trial is behind the *original* schedule. Delays can occur in any phase of the study/clinical trial, including subject enrollment, analysis of study/clinical trial results, or submission of the final report to the FDA. Whereas the *original* schedule — not a revised schedule — serves as the basis for defining a study/clinical trial as *delayed*, each phase of the study/clinical trial will be considered in its own right. If the applicant has one delayed phase, but gets back on schedule during the next phase, the delayed status will no longer apply.

- *Terminated* — The applicant ended the study/clinical trial before completion and has not yet submitted a final report to the FDA.

- *Submitted* — The applicant has concluded or terminated the study/clinical trial and has submitted a final report to the FDA, but the FDA has not yet notified the applicant in writing that the PMR/PMC has been fulfilled or that the PMR/PMC has been released.

Closed Status Categories:

- *Fulfilled* — The applicant has submitted the final report for the PMR/PMC, and upon review of the final report, the FDA has notified the applicant in writing that the terms of the PMR/PMC have been met.

- *Released* — The FDA has informed the applicant in writing that it has been released from its obligation to conduct the study/clinical trial.

When validating the reported status and explanation of status, be aware that the status of a PMR/PMC is based upon the ***original*** schedule milestones set forth in the approval letter or the appropriate PMR/PMC letter if separate from an approval action. Even if the FDA has agreed to or acknowledged revised schedule milestones with the applicant, the applicant must still be held to the original schedule and can be considered *delayed* according to the original schedule. Applicants are likewise instructed in the guidance for industry *Reports on the Status of Postmarketing Study Commitments — Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997*[9] to categorize the status of a PMR/PMC according to the original schedule milestones. FDAAA does not include provisions to amend milestone dates.

Applicant-Reported Status: Enter the status of each open PMR/PMC as provided by the applicant in the ASR. Enter *not reported* if no status is provided by the applicant.

Actual Status per FDA Review: Enter the actual status of the PMR/PMC as determined by FDA review of the ASR and other available information. Use only one of the status categories defined above.

Revised Schedule Milestones: If the applicant has included revised schedule milestones in the ASR, enter *Yes*, otherwise enter *No*. Note that although these milestones are reported, they are not the basis for defining the current status of PMRs/PMCs.

Explanation of Actual Status: The explanation of status is a brief explanation about how the study/trial is progressing in reference to the original projected schedule

[9] We update guidances periodically. To make sure you have the most recent version of a guidance, check the FDA Drugs guidance Web page at http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

milestones. Enter the correct explanation of status as verified by the FDA. If there is no disagreement with the applicant-provided explanation of status, enter it here using the standard terminology below when applicable. For PMRs/PMCs where there is disagreement or information was not reported, provide the corrected explanation of status in its entirety and the reasons why you disagree with the applicant-reported status and/or explanation of status.

For pending, submitted, and fulfilled or released PMRs/PMCs, the standard explanation of status is as follows:

- **Pending:** "The study/trial has not begun but does not meet the criterion for delayed."
- **Submitted:** "The final report was submitted to FDA on <Insert Date>."
- **Released:** "The <PMR/PMC> was released per letter dated <Insert Date>."
- **Fulfilled:** "The <PMR/PMC> was fulfilled per letter dated <Insert Date>."

For ongoing or delayed PMRs/PMCs, consider including the following when providing an explanation of status:

- **Ongoing:** Include the number of subjects enrolled if reported.
- **Delayed:** Include the original milestone date missed and the reason(s) the study/trial is delayed.

Note: *Be aware that the explanation of status you provide for all Pediatric Research Equity Act PMRs and all other PMRs/PMCs with a status of delayed or terminated will be made publicly available on the PMR/PMC Web site (http://www.accessdata.fda.gov/scripts/cder/pmc/index.cfm). Please ensure that there is no proprietary information (e.g., IND numbers, personal privacy information, or references to unapproved formulations of the same drug or other unapproved drug products) included in the corrected explanation of status.*

The corrected status and/or explanation of status, as well as the rationale behind the correction(s), should be communicated to the applicant so that it knows how to report the status and/or explanation of status in the next ASR. You may also use this section of the form to provide the actual statuses and/or explanations of status for open PMRs/PMCs that were not, but should have been, reported in the ASR.

Note: *Because of the implications on future enforcement ability under FDAAA, before communicating with the applicant regarding delays or discrepancies concerning the application with FDAAA-related PMRs, consult with the division safety regulatory project manager, the division deputy director for safety, and the Office of Compliance to obtain the appropriate regulatory language.*

Document Processing and Archiving: Obtain sign-off as determined at the division level and process the form in the document management system. For NDAs, the ASR Review Form is processed in the Document Archiving, Reporting, and Regulatory

Tracking System as FRM-ADMIN-18. In RMS-BLA, the form is entered under communications as a review memo.

Before processing, attach the relevant pages of the ASR to the ASR Review Form and form FDA 2252. For paper submissions, this process will require scanning the original document.

Contact Information: If you have any questions regarding the form or these instructions, please contact the Postmarketing Requirements and Commitment Program Coordinator in the OND Immediate Office at (301) 796-0700.